



Docket No.: C1039.70077US00  
(PATENT)

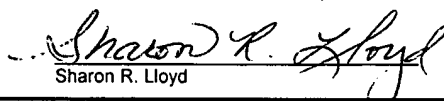
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Arthur M. Krieg  
Serial No.: 10/619279  
Confirmation No.: 8248  
Filed: July 14, 2003  
For: IMMUNOSTIMULATORY NUCLEIC ACID MOLECULES  
Examiner: J.L. Epps Ford  
Art Unit: 1633

Certificate of Mailing Under 37 CFR 1.8(a)

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as First Class Mail, in an envelope addressed to: MAIL STOP Issue Fee, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: February 22, 2007

  
Sharon R. Lloyd

TRANSMITTAL LETTER

**Mail Stop Issue Fee**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

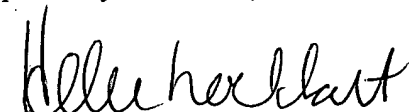
Enclosed are the following items for filing in connection with the above-referenced Patent Application:

1. Application for Patent Term Adjustment Under 37 CFR § 1.705
2. Exhibits 1-5
3. Check in the amount of \$200.00
4. Return Receipt Postcard.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. C1039.70077US00.

Dated: February 22, 2007

Respectfully submitted,

By   
Helen C. Lockhart  
Registration No.: 39,248  
WOLF, GREENFIELD & SACKS, P.C.  
Federal Reserve Plaza  
600 Atlantic Avenue  
Boston, Massachusetts 02210-2206  
(617) 646-8000



*Handwritten signature/initials*

DOCKET NO.: C1039.70077US00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Krieg et al.  
Serial No.: 10/619,279  
Confirmation No.: 8248  
Filed: July 14, 2003  
For: IMMUNOSTIMULATORY NUCLEIC ACID MOLECULES  
Examiner: Janet L. Epps Ford  
Art Unit: 1633

**CERTIFICATE OF MAILING UNDER 37 CFR §1.8(a)**

The undersigned hereby certifies that this document is being placed in the United States mail with first-class postage attached, addressed to MAIL STOP Issue Fee, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the 22<sup>nd</sup> day of February, 2007.

*Sharon R. Lloyd*  
Sharon R. Lloyd

**Mail Stop Issue Fee**  
Commissioner For Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**APPLICATION FOR PATENT TERM ADJUSTMENT UNDER 37 CFR §1.705**

Sir:

Applicants file this Application for Patent Term Adjustment under 37 CFR §1.705(b) requesting reconsideration of the patent term adjustment (PTA) determination for serial number 10/619,279. Applicants provide herein a statement of the facts involved specifying the correct PTA and the basis under 37 CFR §1.702 for the PTA adjustment, relevant dates for which the adjustment is sought, and the adjustment to which the patent is entitled.

1. A Notice of Allowance and PTA calculation were mailed on January 24, 2007 from the US Patent and Trademark Office (USPTO) for US 10/619,279 (Copy enclosed herewith as Exhibit 1).

2. Applicants were accorded a PTA of 580 days for delays occurring at the USPTO.

3. The PTA was also reduced by 55 days based on an alleged delay in term by action of Applicants that took place in the period of May 9, 2006 through July 3, 2006.

4. A restriction requirement was mailed from the Office on April 5, 2006, setting a shortened statutory period for reply of one month (Copy enclosed herewith as Exhibit 2).

5. A reply to the restriction requirement was filed by Applicant on May 5, 2006 and received by the Office on May 9, 2006. (Copy enclosed herewith as Exhibit 3).

6. A preliminary amendment, modifying the claims consistent with the restriction requirement was filed by Applicant on June 29, 2006 and received by the Office on July 3, 2006 (referred to hereafter as the document filed in the USPTO on July 3, 2006, copy enclosed herewith as Exhibit 4).

7. The document filed in the USPTO on July 3, 2006 is listed on PAIR as a Supplemental Response.

8. Applicant submits that the document filed in the USPTO on July 3, 2006 was a preliminary amendment rather than a supplementary response.

9. According to 37 CFR §1.115 (a) a preliminary amendment is "an amendment that is received in the Office (§1.6) on or before the mail date of the first Office action under §1.104."

10. According to 37 CFR §1.104 an Examiner "shall make a thorough study thereof and shall make a thorough investigation of the prior art relating to the subject matter of the claimed invention. The examination shall be complete with respect to both compliance of the application or patent under reexamination with the applicable statutes and rules and to the patentability of the invention as claimed, as well as with respect to matters of form, unless otherwise indicated."

11. The restriction requirement did not provide a thorough examination of the claims including a thorough study of the prior art. Such an examination was conducted after Applicant elected claims for examination and was the subject matter of the Office action mailed on September 21, 2006 (Copy enclosed as Exhibit 5).

12. Applicant submitted a response to the restriction requirement. The response to restriction requirement was complete. The document filed in the USPTO on July 3, 2006 was not a supplemental response to the restriction requirement. Rather it was a preliminary amendment which voluntarily modified the scope of the claims, consistent with the species elected in the restriction requirement. The claims were not required to be amended by the restriction requirement.

13. Under 37 CFR §1.704(c), particular circumstances are delineated that are considered to constitute a failure of the Applicant to engage in reasonable efforts to conclude processing or

examination of an application and that result in a reduction of the period of PTA adjustment set forth in 37 CFR §1.703. The specific circumstances, which are set out in subsections of 37 CFR §1.704(c), include in part, paragraph 6, which reads:

Submission of a preliminary amendment or other preliminary paper less than one month before the mailing of an Office action under 35 USC 132 or notice of allowance under 35 USC 151 that requires the mailing of a supplemental Office action or notice of allowance, in which case the period of adjustment set forth in §1.703 shall be reduced...

14. Applicant submits that the document filed in the USPTO on July 3, 2006 was a preliminary amendment, which was filed more than one month prior to a first substantive Office action and did not necessitate the filing of a supplemental Office action. The preliminary amendment was received by the Office more than one month prior to the issuance of a first Office Action. The first Office Action was mailed from the Office on September 21, 2006. The filing of the preliminary amendment did not necessitate the mailing of a supplemental office action. In fact, the first Office Action addressed the claims as they were amended in the preliminary amendment. The preliminary amendment, amended the scope of the claims, consistent with the restriction requirement. The amendments made in the preliminary amendment were consistent with Applicant's reasonable efforts to conclude processing and examination of the application.

15. The specific circumstances, which are set out in subsections of 37 CFR §1.704(c), also include in part, paragraph 8, which reads:

Submission of a supplemental reply or other paper, other than a supplemental reply or other paper expressly requested by the examiner, after a reply has been filed, in which case the period of adjustment set forth in § 1.703 shall be reduced by the number of days, if any, beginning on the day after the date the initial reply was filed and ending on the date that the supplemental reply or other such paper was filed.

16. Under 37 CFR §1.704(a), when calculating the PTA adjustment, the period of adjustment of the term of a patent shall be reduced by a period equal to the period of time during which the applicant failed to engage in reasonable efforts to conclude prosecution.

17. Under 37 CFR §1.704(b), the Applicant is deemed to have failed to engage in reasonable efforts to conclude processing or examination of an application if a reply to any notice or action by the Office is not filed within three months. Specifically, 37 CFR §1.704(b) reads:

An applicant shall be deemed to have failed to engage in reasonable efforts to conclude processing or examination of an application of the cumulative total of any periods of time in excess of three months that are taken to reply to any notice or action by the Office making any rejection, objection, argument, or other request measuring such three month period from the date the notice was mailed or given to the applicant, in which case the period of adjustment set forth in §1.703 shall be reduced by the number of days, if any, beginning on the day after the date that is three months after the date of mailing or transmission of the Office communication notifying the applicant of the rejection, objection, argument, or other request and ending on the date the reply was filed. The period, or shortened statutory period, for reply that is set in the Office action or notice has no effect on the three-month period set forth in this paragraph.

18. Applicant submits that the reply causing the PTA reduction made by Applicant was both mailed and received by the Office within the three month period set forth in the above quoted paragraph. Although the Examiner had set a shortened statutory period for reply to a restriction requirement of one month, Applicant filed the reply to restriction requirement and preliminary amendment within three months of the mailing date of the restriction requirement. Thus, even if the preliminary amendment were considered to be a supplemental amendment, the document was filed within the three month period of time specified within the rules.

19. Under 37 CFR §1.704(b) Applicant's response to Office action if filed within three months of the mailing date of the Office action will not result in a reduction in PTA, regardless of whether an Examiner has set a shortened statutory period for reply.

20. In view of the fact that the document filed in the USPTO on July 3, 2006 was filed within three months of the restriction requirement, more than one month before the first office action, did not necessitate the mailing of a supplemental office action and was not a supplementary amendment, but rather a preliminary amendment, Applicant submits that the PTA should not be reduced by the 55 days from May 9, 2006 through July 3, 2006 time of the filing of the preliminary amendment and respectfully request PTA reconsideration.

21. A terminal disclaimer was not filed in the instant case and the patent is not subject to a terminal disclaimer.

22. There were no circumstances constituting a failure to engage in reasonable efforts to conclude processing or examination of such application as set forth in §1.704.

Conclusion

Applicants provide above herein a statement of the facts involved specifying the correct PTA and the basis under 37 CFR §1.702 for the PTA adjustment, relevant dates for which the adjustment is sought, and the adjustment to which the patent is entitled. Applicants have also indicated that the patent is not subject to a terminal disclaimer.

In view of the fact that the preliminary amendment was filed within three months of the restriction requirement, more than one month before the first office action, did not necessitate the mailing of a supplemental office action and was not a supplementary amendment, Applicants submit that the 55 days from May 9, 2006 through July 3, 2006 time of the filing of the preliminary amendment, should not be charged against the PTA in this case and request reconsideration of the PTA and its adjustment from 525 days to 580 days.

Applicants submit herewith the fee of \$200.00 for filing an application for patent term adjustment as set forth in 37 CFR §1.18(e). If there is an additional fee occasioned by this application and request that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

By:



Helen C. Lockhart, Ph.D., Reg. No.: 39,248  
Wolf, Greenfield & Sacks, P.C.  
600 Atlantic Avenue  
Boston, Massachusetts 02210-2206  
Telephone: (617) 646-8000

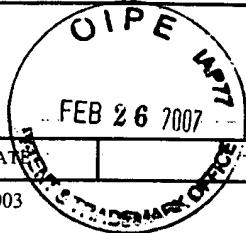
Docket No.: C1039.70077US00  
Date: February 22, 2007



# UNITED STATES PATENT AND TRADEMARK OFFICE

EXHIBIT 1

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov



APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/619,279	07/14/2003	Arthur M. Krieg	C1039.70077US00	8248

7590

01/24/2007

Helen C. Lockhart  
Wolf, Greenfield & Sacks, P.C.  
Federal Reserve Plaza  
600 Atlantic Avenue  
Boston, MA 02210

EXAMINER	
EPPS FORD, JANET L	
ART UNIT	PAPER NUMBER

1633

DATE MAILED: 01/24/2007

## Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 525 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 525 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

EXHIBIT 2

HCL



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/619,279	07/14/2003	Arthur M. Krieg	C1039.70077US00	8248

7590

04/05/2006

Helen C. Lockhart  
Wolf, Greenfield & Sacks, P.C.  
Federal Reserve Plaza  
600 Atlantic Avenue  
Boston, MA 02210

EXAMINER

EPPS FORD, JANET L

ART UNIT

PAPER NUMBER

1633

DATE MAILED: 04/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

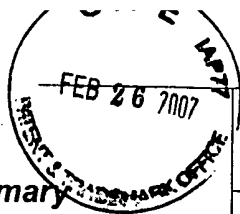
Confirmation	<input type="checkbox"/>	Initials
Docketing	<input checked="" type="checkbox"/>	<i>Pa</i>
05/05/06		

HCL

DOCKETED  
APR 11 2006



# Office Action Summary



Application No.

10/619,279

Applicant(s)

KRIEG, ARTHUR M.

Examiner

Anne Marie S. Wehbe

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 42-57 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 42-57 are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_.

***Election/Restriction***

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 46-47, drawn to a number of permutations and/or combinations of X1, X2, and X3, and X4 as required for the generic formula as set forth in the linking claim 42.

Applicant is required to elect a specific combination of permutations as required at minimum for the formula, wherein each of the X1-X4 must be identified for a specific nucleotide residue.

Each of the sequences with a specific combination of permutations are distinct in its structure and is expected to generate a sequence dependent immunostimulatory effect.

A search of one specific set of permutations for the formula in the prior art does not necessarily overlap with that of another. Further, due to the specificity in structural requirement for each of the specific set of permutation, a sequence search would also be distinct for its of the encompassed sequences and does not appear to be solely affected by any common structure as set forth in the formula, let alone the fact that the formula encompasses an enormous number of <100 nucleotide containing CpG unmethylated sequences. Therefore, a search of a

Art Unit: 1633

composition comprising anything more than a specific set of permutations is considered to be unduly burdensome to the examiner.

For multiple inventions as set forth in claim 46, claim 42 is identified as the linking claims.

Note that the restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), as listed above. Upon the allowance of the linking claims, the restriction requirement as to the liked invention shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such (claim(s) depending from or including all the limitations of the allowable lining claim(s) is/are presented in a continuation or divisional application, the claims or the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Should a specific set of permutations or combination of X1-X4 be elected, the

Elected set of combination/permutations is generic to a plurality of disclosed patentably distinct species comprising a specific sequence which is claimed specifically and listed in claim 52, and which is encompassed by the elected set of combination/permutations:

Art Unit: 1633

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species from as indicated above, even though this requirement is traversed. Each of the listed species is directed to a specific sequence of nucleotide residues, which may or may not be encompassed by the formula with the elected set of permutations. The claimed invention is drawn to an immunostimulatory composition which is desired to be used in an *in vivo* subject, and thus, has a distinct set of variables affecting consideration and examination of each of the distinct immunostimulatory species of sequence. Thereby, a search and examination of anything more than one of such together for patentability would be unduly burdensome to the examiner.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **571-272-0731**.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center number, which is **571-273-8300**.

**ANNE M. WEHBE, PH.D.**  
**PRIMARY EXAMINER**





Atty Docket No.: C1039.70077US00

WGS Date: x05/05/06

Inventor: Arthur M. Krieg

Filing Date: July 14, 2003

Application No.: 10/619279-Conf. #8248

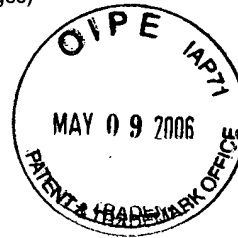
Title: IMMUNOSTIMULATORY NUCLEIC ACID MOLECULES

The USPTO Mail Room acknowledges receipt of the following on the date stamped hereon:

Transmittal Form (1 page)

Response to Restriction Requirement (without Traverse) (2 pages)

Return Receipt Postcard



Via: First Class Mail - Certificate of Mailing Under 37 CFR 1.8(a)

Sender's Initials: HCL/jmw

Date Mailed: May 5, 2006

1022497 1



Docket No.: C1039.70077US00  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Arthur M. Krieg  
Serial No.: 10/619279  
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Examiner: J.L. Epps Ford  
Art Unit: 1633

**Certificate of Mailing Under 37 CFR 1.8(a)**

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as First Class Mail, in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: May 5, 2006

Helen C. Lockhart  
Signature

**TRANSMITTAL LETTER**

**Mail Stop Amendment**  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Enclosed are the following items for filing in connection with the above-referenced Patent Application:

1. Response to Restriction Requirement; and
2. Return Receipt Postcard.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. C1039.70077US00. A duplicate copy of this paper is enclosed.

Dated: May 5, 2006

Respectfully submitted,

By Helen C. Lockhart

Helen C. Lockhart  
Registration No.: 39,248  
WOLF, GREENFIELD & SACKS, P.C.  
Federal Reserve Plaza  
600 Atlantic Avenue  
Boston, Massachusetts 02210-2206  
(617) 646-8000

**WGS Date: x05/05/06**

Docket No.: C1039.70077US00.  
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Applicant: Arthur M. Krieg  
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Dated: May 5, 2006

[Signature]  
Signature

**RESPONSE TO RESTRICTION REQUIREMENT**

**Mail Stop Amendment**  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In response to the restriction requirement set forth in the Office Action mailed April 5, 2006, Applicant hereby elects  $X_1 = G$ ,  $X_2 = T$ ,  $X_3 = T$ , and  $X_4 = T$  for continued examination.

**REMARKS**

In response to the Restriction Requirement, Applicants have elected to prosecute  $X_1 = G$ ,  $X_2 = T$ ,  $X_3 = T$ , and  $X_4 = T$ .


Having made this election, Applicants expressly reserve the right to file one or more divisional applications on the subject matter of the nonelected claims.

**CONCLUSION**

If this response is not considered timely filed and if the extension of time is otherwise absent or incorrect, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Dated: May 5, 2006

Respectfully submitted,

By   
Helen C. Lockhart  
Registration No.: 39,248  
WOLF, GREENFIELD & SACKS, P.C.  
Federal Reserve Plaza  
600 Atlantic Avenue  
Boston, Massachusetts 02210-2206  
(617) 646-8000

WGS Date: x05/05/06



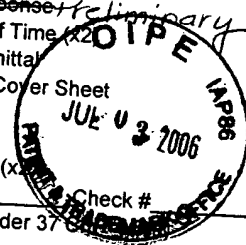
Serial No. 10/619,279 Docket No. C1039-70077US00 Initials HCL  
 Title Immunostimulatory Nucleic Acid Molecules Conf No 8248  
 Applicant(s) Arthur M. Kricg Filing Date 7-14-03 WGS Date ND

The USPTO Mail Room acknowledges receipt of the following on the date stamped hereon:

- |   |   |
|---|---|
| <input type="checkbox"/> Mailing by Express Mail (37 CFR 1.10)  | <input type="checkbox"/> Provisional Application Cover Sheet                                |
| Express Mail Label No. _____  | <input type="checkbox"/> Inf. Dis. Statement (SB/08 or 1449)                                |
| <input type="checkbox"/> Utility Patent Application   | <input type="checkbox"/> Copies of Cited Refs. Encl.  |
| <input type="checkbox"/> Non-Provisional <input type="checkbox"/> Provisional                                     | <input type="checkbox"/> US <input type="checkbox"/> Foreign <input type="checkbox"/> Other |
| Tot Pages _____ Tot Claims _____  | <input type="checkbox"/> RCE Transmittal  |
| ( pgs) Spec. ( pgs) Abstract ( pgs) Claims  | <input type="checkbox"/> Copy of Notice to File Missing Parts                               |
| <input type="checkbox"/> Design Patent Application and Transmittal  | <input checked="" type="checkbox"/> Amendment/Response <i>Preliminary</i>                   |
| <input type="checkbox"/> Declaration(s) <input type="checkbox"/> new <input type="checkbox"/> copy from prior app | <input type="checkbox"/> Petition for Ext. of Time (x2)                                     |
| <input type="checkbox"/> Drawings Sheets _____ Figures _____  | <input type="checkbox"/> Issue Fee Transmittal  |
| <input type="checkbox"/> Formal <input type="checkbox"/> Informal   | <input type="checkbox"/> Assignment and Cover Sheet   |
| <input type="checkbox"/> Utility Patent Application Transmittal   | <input type="checkbox"/> Notice of Appeal   |
| <input type="checkbox"/> Fee Calculation Sheet (x2)   | <input type="checkbox"/> Brief  |
| <input checked="" type="checkbox"/> Application Data Sheet - <i>Supplemental</i>                                  | <input checked="" type="checkbox"/> Transmittal Letter (x2)                                 |
| <input type="checkbox"/> Power of Attorney  | <input type="checkbox"/> Check for \$ _____ Check # _____                                   |
| <input type="checkbox"/> Request for Approval and Entry of Drawings   | <input checked="" type="checkbox"/> Cert. of Mailing under 37 CFR 1.101                     |
| <input type="checkbox"/> Other _____  |   |

DATE MAILED June 29, 2006

PAT





DOCKET NO.: C1039.70077US00


IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Arthur M. Krieg  
Serial No.: 10/619,279  
Confirmation No.: 8248  
Filed: July 14, 2003  
For: IMMUNOSTIMULATORY NUCLEIC ACID MOLECULES  
Examiner: J. L. Epps Ford  
Art Unit: 1633

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CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

The undersigned hereby certifies that this document is being placed in the United States mail with first-class postage attached, addressed to MAIL STOP AMENDMENT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the 29 day of June, 2006.

  
Helen C. Lockhart, Ph.D., Reg. No. : 39,248

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MAIL STOP AMENDMENT

Commissioner For Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

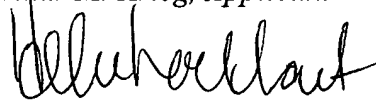
Transmitted herewith are the following documents:

- ☒ Preliminary Amendment
- ☒ Supplemental Application Data Sheet
- ☒ Return Receipt Postcard

If the enclosed papers are considered incomplete, the Mail Room and/or the Application Branch is respectfully requested to contact the undersigned at (617) 646-8000, Boston, Massachusetts.

A check is not enclosed. If a fee is required, the Commissioner is hereby authorized to charge Deposit Account No. 23/2825. A duplicate of this sheet is enclosed.

Respectfully submitted,  
*Arthur M. Krieg, Applicant*

By:   
Helen C. Lockhart, Ph.D., Reg. No.: 39,248  
Wolf, Greenfield & Sacks, P.C.  
600 Atlantic Avenue  
Boston, Massachusetts 02210-2206  
Telephone: (617) 646-8000

Docket No.: C1039.70077US00  
Date: June 29, 2006  
xNDDx



Docket No.: C1039.70077US00  
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Arthur M. Krieg  
Serial No.: 10/619279  
Confirmation No.: 8248  
Filed: July 14, 2003  
For: IMMUNOSTIMULATORY NUCLEIC ACID MOLECULES  
Examiner: J. L. Epps Ford  
Art Unit: 1633

**Certificate of Mailing Under 37 CFR 1.8(a)**

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as First Class Mail, in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: June 29, 2006

Signature

**Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450**

**PRELIMINARY AMENDMENT**

Dear Sir:

## INTRODUCTORY COMMENTS

Prior to examination on the merits, please amend the above-identified U.S. patent application as follows:

**Amendments to the Specification** begin on page 2 of this paper.

**Amendments to the Claims** begin on page 3 of this paper.

**Remarks/Arguments** begin on page 7 of this paper.

**AMENDMENTS TO THE SPECIFICATION**

Please replace the paragraph immediately following the heading **Related Applications** on page 1, line 5, with the following paragraph:

This application is a continuation of co-pending U.S. Patent Application serial number 09/337,893 filed on June 21, 1999 and now pending which is a divisional of U.S. Serial No. 08/960,774, filed October 30, 1997, now issued as US 6,239,116 B1 ~~which is a continuation in part of U.S. Serial No. 08/738,652, filed October 30, 1996, now issued as US 6,207,646 B1, which is a continuation in part of U.S. Patent Application serial number 08/386,063, filed February 7, 1995 now issued as U.S. Patent No. 6,194,388, which is a continuation in part of U.S. Patent Application 08/276,358, filed July 15, 1994 which is now abandoned~~, each of which are incorporated herein by reference in their entirety.

AMENDMENTS TO THE CLAIMS

A complete listing of claims is presented below with insertions indicated by underlining and deletions indicated by strikeouts and/or double bracketing. Please replace all prior versions, and listings, of claims in the application with the following list of claims:

1-41 (Canceled)

42. (Currently Amended) A ~~composition comprising~~ an immunostimulatory nucleic acid, having a sequence including at least the following formula:

5' ~~TCNTX<sub>1</sub>X<sub>2</sub>CpGX<sub>3</sub>X<sub>4</sub>~~ 3' 5' TCGTCGTTTTGTCGTTTTGTCGTT 3' (SEQ ID No. 46)

~~wherein X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>, and X<sub>4</sub> are nucleotides, N is a nucleic acid sequence composed of from about 0-25 nucleotides, wherein at least one nucleotide has a phosphate backbone modification, and wherein the nucleic acid has less than or equal to 100 nucleotides, and wherein C is unmethylated.~~

43. (Currently Amended) The ~~composition~~ immunostimulatory nucleic acid of claim 42, wherein at least one nucleotide has a phosphate backbone modification and wherein the phosphate backbone modification is a phosphorothioate or phosphorodithioate modification.

44. (Currently Amended) The ~~composition~~ immunostimulatory nucleic acid of claim 42, wherein at least one nucleotide has a phosphate backbone modification and wherein the phosphate backbone modification occurs at the 5' end of the nucleic acid.

45. (Currently Amended) The ~~composition~~ immunostimulatory nucleic acid of claim 42, wherein at least one nucleotide has a phosphate backbone modification and wherein the phosphate backbone modification occurs at the 3' end of the nucleic acid.

46-50. (Canceled Herewith)

51. (Currently Amended) The ~~composition~~ immunostimulatory nucleic acid of claim 42, wherein the immunostimulatory nucleic acid is ~~8 to~~ less than 40 nucleotides in length.

52. (Canceled Herewith).

53. (Currently Amended) A method for stimulating an immune response, comprising administering to a subject the ~~composition~~ immunostimulatory nucleic acid of claim 42 in an effective amount to stimulate an immune response.

54. (Previously Presented) The method of claim 53, wherein the subject has or is at risk of developing asthma.

55. (Previously Presented) The method of claim 53, wherein the subject has or is at risk of developing allergy.

56. (Previously Presented) The method of claim 53, wherein the subject has or is at risk of developing cancer.

57. (Previously Presented) The method of claim 53, wherein the subject has or is at risk of developing infectious disease.

58. (New) The immunostimulatory nucleic acid of claim 42, wherein the immunostimulatory nucleic acid has a sequence consisting of TCGTCGTTTTGTCGTTTTGTCGTT (SEQ ID No. 46).

59. (New) The immunostimulatory nucleic acid of claim 58, wherein each internucleotide linkage has a phosphorothioate modification.

60. (New) The immunostimulatory nucleic acid of claim 58, further comprising an antigen.

61. (New) The immunostimulatory nucleic acid of claim 60, wherein the antigen is a vaccine and further comprising a conventional adjuvant.

62. (New) A method for treating cancer, comprising administering to a subject the immunostimulatory nucleic acid of claim 58 in an effective amount to treat cancer.

63. (New) A method for treating cancer, comprising administering to a subject the immunostimulatory nucleic acid of claim 59 in an effective amount to treat cancer.

64. (New) The method of claim 62, wherein the immunostimulatory nucleic acid is administered prior to along with or after administration of a chemotherapy.

65. (New) The method of claim 63, wherein the immunostimulatory nucleic acid is administered prior to along with or after administration of a chemotherapy.

66. (New) The method of claim 62, wherein the immunostimulatory nucleic acid is administered prior to along with or after administration of an immunotherapy.

67. (New) The method of claim 63, wherein the immunostimulatory nucleic acid is administered prior to along with or after administration of an immunotherapy.

68. (New) The method of claim 62, wherein the immunostimulatory nucleic acid is administered by injection.

69. (New) A method for generating an antibody in a mammal, comprising, administering to a mammal an effective amount of the immunostimulatory nucleic acid of claim 58 as an artificial adjuvant and an antigen to generate antibodies in the mammal.

70. (New) The method of claim 69, wherein the mammal is a human.

71. (New) The method of claim 69, further comprising isolating the antibody from the mammal.

72. (New) The method of claim 62, wherein the cancer is brain, lung, ovary, breast, prostate, or colon cancer

73. (New) The method of claim 62, wherein the cancer is a carcinomas or sarcoma.

74. (New) The immunostimulatory nucleic acid of claim 42, wherein the immunostimulatory nucleic acid is formulated as a composition with a pharmaceutically acceptable carrier.



**REMARKS**

Applicant has amended claim 42 to recite a specific SEQ ID NO. (SEQ ID NO.: 46) that was pending in now canceled claim 52. As a result of the amendment to claim 42 claims 46-50 and 52 have been canceled and claims 43-45, 51 and 53 have been amended to be consistent with the new scope of claim 42. SEQ ID NO.: 46 falls within the scope of the invention elected for prosecution in response to the restriction requirement.

New dependent claims 58-74 have been added. Support for the limitations are found in pending claims or now canceled claims as well as throughout the specification. Support for claims 60 and 61 directed to an antigen (a vaccine is minimally comprised of an antigen) and conventional adjuvants is found on page 52 lines 14-20. Support for administration of a chemotherapy or immunotherapy is found on page 53 lines 5-8. Support for administration by injection is found on page 54 lines 10-11. Support for the different types of cancers is found on page 14 lines 2-4.

Support for a method of generating an antibody in a mammal by administering the composition as an artificial adjuvant is found in the specification in the summary of the invention, page 8 and on page 17 lines 10-11.

Applicant has also amended the related applications paragraph on the first page of the specification in view of the changes to the claims to reflect that the earliest effective priority date of the claims currently pending and directed to SEQ ID NO.: 46 is October 30, 1997. The claim of priority to US Patent Numbers 6,207,646 and 6,194,388 and US patent application number 08/276,358 has been dropped. An application data sheet reflecting this change has also been filed concurrently. No new matter has been added.

---

**Continuity Information**

This application is a: Continuation  
Claiming priority to:  
Serial Number: 09/337,893  
Filing Date: June 21, 1999  
Status: Pending

Which is a: Divisional  
Claiming priority to:  
Serial Number: 08/960,774  
Filing Date: October 30, 1997  
Status: Issued

~~Which is a:~~ ~~Continuation in part~~  
~~Claiming priority to:~~  
~~Serial Number:~~ 08/738,652  
~~Filing Date:~~ October 30, 1996  
~~Status:~~ Issued

~~Which is a:~~ ~~Continuation in part~~  
~~Claiming priority to:~~  
~~Serial Number:~~ 08/386,063  
~~Filing Date:~~ February 7, 1995  
~~Status:~~ Issued

~~Which is a:~~ ~~Continuation in part~~  
~~Claiming priority to:~~  
~~Serial Number:~~ 08/276,358  
~~Filing Date:~~ July 15, 1994  
~~Status:~~ Abandoned

**Assignee Information (when available)**

Name of Assignee: University of Iowa Research Foundation  
Address: 214 Technology Innovation Center, Oakdale Research Campus  
Iowa City, Iowa 52242



UNITED STATES PATENT AND TRADEMARK OFFICE

EXHIBIT 5

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/619,279

07/14/2003

Arthur M. Krieg

C1039.70077US00

8248

7590

09/21/2006

Helen C. Lockhart  
Wolf, Greenfield & Sacks, P.C.  
Federal Reserve Plaza  
600 Atlantic Avenue  
Boston, MA 02210

EXAMINER

EPPS FORD, JANET L

ART UNIT

PAPER NUMBER

1633

DATE MAILED: 09/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Confirmation	<input type="checkbox"/>	initials
Docketing	<input checked="" type="checkbox"/>	Ca

12/21/06

HCK

DOCKETED  
SEP 28 2006

**Office Action Summary**

FEB 26 2007

Application No.

10/619,279

Applicant(s)

KRIEG, ARTHUR M.

Examiner

Janet L. Epps-Ford

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 03 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 42-74 is/are pending in the application.
- 4a) Of the above claim(s) 62-73 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 42-61 and 74 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) ✓
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) ✓  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Oath/Declaration***

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:  
The specification to which the oath or declaration is directed has not been adequately identified. See MPEP § 602.

### ***Election/Restrictions***

2. Applicant's election of immunostimulatory nucleic acid comprising wherein X1, X2, X3, and X4 are G, T, T, and T respectively as defined in formula: 5'-TCNTX1X2CpGX3X4-3' in the original claim 42, in the reply filed on 5-09-06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 42-57 were the subject of the restriction requirement mailed, 4-05-06. In the reply filed 5-09-06, Applicants made the above election. In the amendment filed 7-03-06, Applicants added new claims 58-74. However, of the newly added claims, claims 58-61, and 74 are directed to the invention as originally presented. Newly added claims 62-73 appear to be directed to non-elected inventions for the reasons given below:

Art Unit: 1633

- a. Claims 62-68, and 72-73 are drawn to a method for treating cancer comprising the administration of the immunostimulatory nucleic acid of SEQ ID NO: 46 in addition to chemotherapy or immunotherapy.
- b. Claims 69-71 are drawn to a method for generating an antibody comprising the administration of an immunostimulatory nucleic acid in combination with an antigen.

The inventions of groups a-b are patentably distinct from the immunostimulatory nucleic acids, and methods for stimulating an immune response as set forth in original claims 42-57, and new claims 58-61 and 74. The methods of groups a-b set forth above are drawn to distinct methods comprising distinct objectives, distinct method steps, distinct reagents, and further comprising the production of distinct outcomes. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed comprise distinct objectives, distinct method steps, distinct reagents, and further comprising the production of distinct outcomes. Moreover, the newly added methods require different considerations under 35 USC 112, 1<sup>st</sup> paragraph. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

### ***Double Patenting***

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Omum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 42-61 and 74 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-49 of U.S. Patent No. 6,239,116 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to immunostimulatory nucleic acids having the nucleotide sequence as set forth in SEQ ID NO: 46, and to a generic methods for stimulating an immune response, however the issued claims which are drawn to a method for stimulating IL-6, and the method of stimulating natural killer cells represent a species of the broader method of the instant claims. The issued claims also disclose SEQ ID NO: 46 of the instant claims as one of the immunostimulatory nucleic acids used in the issued methods. Therefore, since the

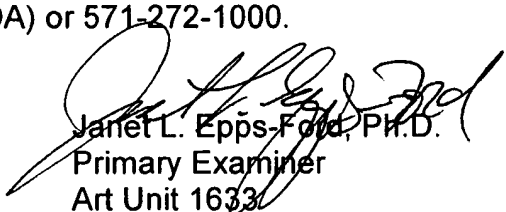
Art Unit: 1633

methods of the issued claims represent a species of the broader instant claims, the issued claims are considered to anticipate the claims of the instant application.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Janet L. Epps-Ford, Ph.D.  
Primary Examiner  
Art Unit 1633

JLE



FORM PTO-1449/A and B (Modified)

APPLICATION NO.: 10/679,279

ATTY. DOCKET NO.: C1039.70077US00

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

FILING DATE: July 14, 2003

CONFIRMATION NO.: 8248

APPLICANT: Arthur M. Krieg, et al.

GROUP ART UNIT: 1632

EXAMINER: Not yet assigned

Sheet 1 of 4

## U.S. PATENT DOCUMENTS

Examiner	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication or of issue of Cited Document MM-DD-YYYY
		Number	Kind Code		
JE	*	5,417,972		Bhat et al.	05/23/1995
	*	5,445,938		Hanai et al.	08/29/1995
	*	5,491,088		Hellstrom et al.	02/13/1996
	*	5,679,647	B1	Carson et al.	10/21/1997
	*	5,756,097		Landucci et al.	05/26/1998
	*	5,780,448	B1	Davis	07/14/1998
	*	5,837,243		Deo et al.	11/17/1998
	**	6,225,292	B1	Raz, et al.	05/01/2001
	*	6,426,334	B1	Agrawal et al.	07/30/2002
	**	6,514,948	B1	Raz, et al.	02/04/2003
	**	6,534,062	B2	Krieg, et al.	03/18/2003
	**	6,552,006	B2	Raz et al.	04/22/2003
	**	6,562,798	B1	Schwartz	05/13/2003
	**	6,589,940	B1	Raz et al.	07/08/2003
	**	6,610,661	B1	Carson et al.	08/26/2003
	**	6,653,292	B1	Krieg et al.	11/25/2003
	**	US 2001/0046967	A1	Van Nest	11/29/2001
	**	US 2002/0028784	A1	Van Nest	03/07/2002
	**	US 2002/0055477	A1	Nest	05/09/2002
	**	US 2002/0098199	A1	Nest et al.	07/25/2002
	**	US 2002/0107212	A1	Van Nest et al.	08/08/2002
	**	US 2002/0142978	A1	Van Nest et al.	10/03/2002
	**	US 2002/0156033	A1	Raz et al.	10/24/2002
	**	US 2003/0049266	A1	Bratzler et al.	03/13/2003
	**	US 2003/0050263	A1	Fearon et al.	03/13/2003
	**	US 2003/0078223	A1	Krieg et al.	04/24/2003
	**	US 2003/0092663	A1	Raz et al.	05/15/2003
	**	US 2003/0109469	A1	Raz	06/12/2003
	**	US 2003/0119773	A1	Carson et al.	06/26/2003
	**	US 2003/0129251	A1	Raz et al.	07/10/2003
	**	US 2003/0133988	A1	Van Nest et al.	07/17/2003
	**	US 2003/0143213	A1	Fearon et al.	07/31/2003
	**	US 2003/0147870	A1	Raz et al.	08/07/2003
	**	US 2003/0175731	A1	Raz et al.	09/18/2003
	**	US 2003/0186921	A1	Rearon et al.	10/02/2003
JE	**	US 2003/0199466	A1	Fearon et al.	10-23-2003

CANCELLED

JAN 09 2004

<b>FORM PTO-1449/A and B (Modified)</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>		APPLICATION NO.: 10/619,279		ATTY. DOCKET NO.: C1039.70077US00		
		FILING DATE: July 14, 2003		CONFIRMATION NO.: 8248		
		APPLICANT: Arthur M. Krieg, et al.				
		GROUP ART UNIT: 1632		EXAMINER: Not yet assigned		
Sheet	26	of	4			

**U.S. PATENT DOCUMENTS**

Examiner's Initials	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication or of issue of Cited Document MM-DD-YYYY
		Number	Kind Code		
JE	**	US 2003/0212028	A1	Raz et al.	11-13-2003
JE	**	US 2003/0216340	A1	Van Nest et al.	11-20-2003

**FOREIGN PATENT DOCUMENTS**

Examiner's Initials	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document (not necessary)	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
		Office/ Country	Number	Kind Code			
JE	*	WO	96/02560	A1	University of NC at Chapel Hill	02/01/1996	
JE	B1	WO	99/62923	A2	Dynavax Tech. Corp.	12/09/1999	
JE	B2	WO	00/20039	A1	Regents of the University of CA	04/13/2000	
JE	B3	WO	00/62787	A1	Regents of the University of CA	10/26/2000	

**OTHER ART — NON PATENT LITERATURE DOCUMENTS**

Examiner's Initials	Cite No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)	
JE	*	AGGARWAL, S.K. et al., "Cell-Surface-Associated Nucleic Acid in Tumorigenic Cells Made Visible with Platinum-Complexes by Electron Microscopy", <i>Proc. Nat. Acad. Sci. USA</i> , March 1975, Pages 928-932, Vol. 72, No. 3		
JE	*	BERNHARD, M., et al., "Monocyte Macrophage Mediated Antibody Dependent and Independent Cell Mediated Cytotoxicity in Normals and Cancer Patients, ABSTRACT, Proceedings of AACR and ASCO, 22:372, c-159		
JE	*	COHEN, J., et al., "IL-12 Deaths: Explanation and a Puzzle", <i>Science</i> , 10:270:5238:908		
JE	*	COSSUM, P., et al., "Pharmacokinetics of a <sup>14</sup> C-Labeled Phosphorothioate Oligonucleotide, ISIS 2105, after Intradermal Administration to Rats", <i>The Journal of Pharmacology and Experimental Therapeutics</i> , 269:1:89-94, (1993)		
JE	*	DOE, B., et al., "Induction of cytotoxic T lymphocytes by intramuscular immunization with plasmid DNA is facilitated by bone marrow-derived cells", <i>Proc. Natl. Acad. Sci.</i> , 93:8578-8583, (1996)		
JE	*	GATELY, M., et al., "Interleukin-12: A Recently Discovered Cytokine with potential for Enhancing Cell-Mediated Immune Responses to Tumors", <i>Cancer Investigation</i> , 11:4:500-506, (1993)		
JE	*	HAMBLIN, T., et al., "Ex Vivo Activation and Retransfusion of White Blood Cells", <i>Curr Stud Hematol Blood Transf</i> , 57:249-266, (1990)		
JE	*	HARTMANN, G., et al., "CpG DNA: A potent signal for growth, activation, and maturation of human dendritic cells", <i>Proc. Natl. Acad. Sci.</i> , 96:9305-9310, (1999)		
JE	*	KATAOKA, T., et al. "Immunotherapeutic potential in Guinea-Pig Tumor Model of Deoxyribonucleic Acid From Mycobacterium Bovis BCG Complexed with Poly-L-Lysine and Carboxy-Methylcellulose", <i>Jpn J. Med. Sci. Biol.</i> 43:171-182, (1990)		
JE	*	KLINMAN, D.M. et al., "Contribution of CpG Motifs to the Immunogenicity of DNA Vaccines", <i>J. of Immunol.</i> , 1997, Pages 3635-3639, Vol. 158, No. 8, The American Association of Immunologists		
JE	*	KOLITZ, J., et al., "The Immunotherapy of Human Cancer with Interleukin 2: Present Status and Future Directions", <i>Cancer Investigation</i> , 9:5:529-542, (1991)		

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FORM PTO-1449/A and B (Modified)		APPLICATION NO.: 10/619,279	ATTY. DOCKET NO.: C1039.70077US00
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		FILING DATE: May 14, 2003	CONFIRMATION NO.: 8248
		APPLICANT: Arthur M. Krieg, et al.	
GROUP ART UNIT: 1632		EXAMINER: Not yet assigned	
Sheet 3	of 4		

OTHER ART — NON PATENT LITERATURE DOCUMENTS

Examiner's Initials	No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
JE	*	KURAMOTO, E., et al., "In Situ Infiltration of Natural Killer-Like Cell Induced by Intradermal Injection of the Nucleic Acid Fraction from BCG", <i>Microbiol. Immunol.</i> , 33:11:929-940, (1989)	
	*	KURAMOTO, E., et al., "Changes of host cell infiltration into meth a fibrosarcoma tumor during the course of regression induced by injections of a BCG nucleic acid fraction", <i>Int. J. Immunopharmacol.</i> 14:5:773-782, (1992)	
	*	Lacour, J., et al., "Clinical Trials Using Polyadenylic-Polyuridylic Acid as an Adjuvant to Surgery in Treating Different Human Tumors", <i>J of Biological Response Modifiers</i> , 4:538-543, (1985)	
	*	LIPFORD, G.B. et al., "CpG-containing synthetic oligonucleotides promote B and cytotoxic T cell responses to protein antigen: a new class of vaccine adjuvants", <i>Eur. J. Immunol.</i> , 1997, Pages 2340-2344, Vol. 27	
	*	LIPFORD, G.B. et al., "Bacterial DNA as immune cell activator", <i>Inst. of Med. Microb., Immunol. and Hygiene</i> , 1998, Pages 496-500, Elsevier Science	
	*	MASHIBA, H., et al., "In Vitro Augmentation of Natural Killer Activity of Peripheral Blood Cells From Cancer Patients by a DNA Fraction From Mycobacterium Bovis BCG", <i>Jpn J. Med. Sci. Biol.</i> , 41:197-202, (1988)	
	*	MORAHAN, P., et al., "Comparative Analysis of Modulators of Nonspecific Resistance Against Microbial Infections", <i>Immunopharmacology of Infectious Diseases: Vaccine Adjuvants and Modulators of Non-Specific Resistance</i> , 313-324, (1987)	
	*	REISFELD, R., et al., "Monoclonal Antibodies in Cancer Therapy", <i>Clinics in Laboratory Medicine</i> , 12:2:201-216, (1992)	
	*	ROSENBERG, S., et al., "Immunotherapy of Cancer by Systemic Administration of Lymphoid Cells Plus Interleukin-2", <i>Journal of Biological Response Modifiers</i> , 3:501-511, (1984)	
	*	ROSENBERG, S., et al., "Observations on the systemic administration of autologous lymphokine-activated killer cells and recombinant interleukins-2 to patients with metastatic cancer", <i>The New England Journal of Medicine</i> , 113:23:1485-1492, (1985)	
	*	SHIMADA, S., et al., "In Vivo Augmentatio of Natural Killer Cell Activity With A Deoxyribonucleic Acid Fraction of BCG", <i>Jpn J. Cancer Res.</i> , 77:808-816, (1986)	
	*	SHIMADA, S., et al., "Antitumor Activity of the DNA Fraction from Mycobacterium bovis BCG. II> Effects on Various Syngeneic Mouse Tumors", <i>JNCI</i> , 74:3:681-688, (1985)	
	*	STEVENSON, H., et al., "The Treatment of Cancer with Activated Cytotoxic Leukocyte Subsets", <i>Artif Organs</i> , 12:2:128136, 1988	
	*	STULL, R.A. et al., "Antigene, Ribozyme and Aptamer Nucleic Acid Drugs: Progress and Prospects", <i>Pharmaceutical Research</i> , 1995, Pages 465-483, Vol. 12, No. 4, Plenum Publishing Corp.	
	*	SUN, S. et al., "Mitogenicity of DNA from Different Organisms for Murine B Cells", <i>The Journal of Immunology</i> , 1997, Pages 3119-3125, The American Association of Immunologists	
	*	THREADGILL, D.S. et al., "Mitogenic synthetic polynucleotides suppress the antibody response to a bacterial polysaccharide", <i>Vaccine</i> , 1998, Pages 76-82, Vol. 16, No. 1, Elsevier Science Ltd.	
	*	TOPALIAN, S., et al., "Expansion of human tumor infiltrating lymphocytes for use in immunotherapy trials", <i>J of Immunological Methods</i> , 102:127-141, (1987)	
	*	TORPEY III, D., et al., "Effects of Adoptive Immunotherapy with Autologous CD8+ t Lymphocytes on Immunologic Parameters: Lymphocyte Subsets and Cytotoxic Activity", <i>Clinical Immunology and Immunopathology</i> , 68:3:263-272, (1993)	
JE	*	VOGELS, M., et al., "Use of Immune Modulators in nonspecific Therapy of Bacterial Infections", <i>Antimicrobial Agents and Chemotherapy</i> , 36:1:1-5, (1992)	

<b>FORM PTO-1449/A and B (Modified)</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	APPLICATION NO.: 10/619,279	ATTY. DOCKET NO.: C1039.70077US00
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Sheet <b>FEB 26 2007</b> of 4		

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JE	*	WILTROUT, R.H., et al., "Immunomodulation of Natural Killer Activity by Polyribonucleotides", <i>Journal of Biological Response Modifiers</i> , 1985, Pages 512-517, Vol. 4, No. 5, New Raven Press, NY	
JE	*	WOOLDRIDGE, J., et al., "Immunostimulatory Oligodeoxynucleotides Containing CpG Motifs Enhance the Efficacy of Monoclonal Antibody Therapy of Lymphoma", <i>Blood</i> , 89:8:2994-2998, (1997)	
JE	*	WOOLDRIDGE, J.E. et al., "Select Unmethylated CpG Oligodeoxynucleotides Improve Antibody Dependent Cellular Cytotoxicity <i>in Vitro</i> of Both Murine and Human B Cell Lymphomas", <i>Blood</i> , December 1995, Page 2877, Abstract, Vol. 86	
JE	*	WOOLDRIDGE, J.E. et al., "Select unmethylated CpG oligodeoxynucleotide improve antibody dependent cellular cytotoxicity <i>in vitro</i> and <i>in vivo</i> ", Proceedings of the American Association for Cancer Research #3253, March 1996, Page 477, Abstract, Vol. 37	

EXAMINER /Janet Epps Ford/	DATE CONSIDERED 09/18/2006
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#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

\*a copy of this reference is not provided as it was previously cited by or submitted to the office in one of the prior applications, Serial No. 08/386,063, filed February 7, 1995, Serial No. 08/738,652, filed October 30, 1996, Serial No. 09/337,619, filed June 21, 1999, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

\*\* copies of these patents and patent applications are not enclosed pursuant to the waiver by the USPTO of the requirement under 37 C.F.R. 1.98 (a)(2)(i) for patent applications filed after June 30, 2003.

[NOTE - Must provide a copy of any patent, publication, other information listed, even if it was previously submitted to, or cited by, the U.S. Patent Office in an earlier application, unless the earlier application is identified by the IDS and is relied upon for an earlier filing date under 35 U.S.C. §120, and the copy was provided in the earlier application.]



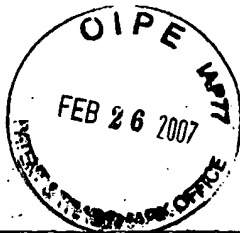
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	APPLICANT Krieg	
FILING DATE July 14, 2003		GROUP Not Yet Assigned

### U.S. PATENT DOCUMENTS

Exam Init	Ref Des	Document No.	Date	Name	Class	Sub Class	FILING DATE If Appropriate
*		3,906,092	09/16/75	Hilleman et al.			
*		5,248,670	09/28/93	Draper et al.	514	44	
*		5,585,479	12/17/96	Hoke et al.	536	24.5	
*		5,663,153	09/02/97	Hutcherson et al.	514	44	
*		5,723,335	03/03/98	Hutcherson et al.	435	375	
*		5,786,189	07/28/98	Locht et al.	435	172.3	
*		5,849,719	12/15/98	Carson et al.	514	44	
*		6,498,148	12/24/02	Raz			



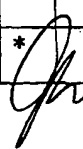
### FOREIGN PATENT DOCUMENTS

	Country & Doc. No. (11)	Pub. Date (43)		Class	Sub Class	Translation Yes No	
*	WO 91/12811	09/05/91	PCT	A61K	31/70		
*	0468520 A3	01/29/92	EPO	A61K	31/70		
*	WO 92/03456	03/05/92	PCT	C07H	15/12		
*	WO 92/18522	10/29/92	PCT	C07H	21/00		
*	WO 92/21353	12/10/92	PCT	A61K	31/70		
*	0302758 81	03/16/94	EPO	C12N	15/37		
*	WO 94/19945	09/15/94	PCT	A01N	43/04		
*	WO 95/05853	03/02/95	Regents of the University of CA				
*	WO 95/26204	10/95	PCT	A61K	48/00		
*	WO 96/02555	02/01/96	PCT				
*	WO 96/35782	11/14/96	Applied Research Systems				
*	WO 97/28259	08/07/97	PCT	C12N	15/00		
*	WO 98/18810	05/07/98	PCT	C07H	21/00		
*	WO 98/37919	09/03/98	PCT	A61K	49/00		
*	WO 98/40100	09/17/98	PCT	A61K	39/39		
*	WO 98/52581	11/26/98	PCT	A61K	35/00		
*	WO 98/14210	04/09/98	PCT	A61K	39/35		



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				APPLICANT Krieg					
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*		WO 98/16247	04/23/98	Regents of the University of CA					
*		WO 98/32462	07/30/98	Wagner et al.					
*		WO 98/49288	11/05/98	Hybridon, Inc.					
*		WO 98/55495	12/10/98	Dynavax Technologies Corp.					
*		WO 99/11275	03/11/99	Regents of the University of CA					
<b>OTHER ART</b> (Including Author, Title, Date, Pertinent Pages, Publication, Etc.)									
*		Adya N et al., Expansion of CREB's DNA recognition specificity by Tax results from interaction with Ala-Ala-Arg at positions 282-284 near the conserved DNA-binding domain of CREB. <i>Proc Natl Acad Sci USA</i> 91(12):5642-6, 7 Jun 1994.							
*		Angier, N., Microbe DNA Seen as Alien By Immune System, <i>New York Times</i> , 4/11/95							
*		Azad RF et al., Antiviral Activity of a Phosphorothioate Oligonucleotide Complementary to RNA of the Human Cytomegalovirus Major Immediate-Early Region. <i>Antimicrobial Agents and Chemotherapy</i> , 37:1945-1954, September, 1993.							
*		Azuma, Biochemical and Immunological Studies on Cellular Components of Tubercle Bacilli, <i>Kekkaku</i> , Vol. 69, 9:45-55, 1992.							
*		Ballas ZK et al., Induction of NK activity in murine and human cells by CpG motifs in oligodeoxynucleotides and bacterial DNA. <i>J Immunol</i> 157(5):1840-5, 1996.							
*		Bayever, E., Systemic Administration of a Phosphorothioate Oligonucleotide with a Sequence Complementary to p53 for Acute Myelogenous leukemia and Myelodysplastic Syndrome: Initial Results of a Phase I Trial, <i>Antisense Res. &amp; Dev.</i> (1993), 3:383-390.							
*		Bennett RM et al., DNA binding to human leukocytes. Evidence for a receptor-mediated association, internalization, and degradation of DNA. <i>J Clin Invest</i> 76(6):2182-90, 1985.							
*		Berg DJ et al., Interleukin-10 is a central regulator of the response to LPS in murine models of endotoxic shock and the Schwartzman reaction but not endotoxin tolerance. <i>J Clin Invest</i> 96(5):2339-47, 1995.							
*		Blanchard DK et al., Interferon-gamma induction by lipopolysaccharide: dependence on interleukin 2 and macrophages. <i>J Immunol</i> 136(3):963-70, 1986.							
*		Blaxter et al., Genes expressed in <i>Brugia malayi</i> infective third stage larvae. <i>Molecular and Biochemical Parasitology</i> , 77:77-93.							
*		Boggs RT et al., Characterization and modulation of immune stimulation by modified oligonucleotides. <i>Antisense Nucleic Acid Drug Dev</i> 7(5):461-71, Oct 1997.							
*		Branda RF et al., Amplification of antibody production by phosphorothioate oligodeoxynucleotides. <i>J. Lab Clin Med</i> 128(3):329-38, Sep 1996.							
*		Branda et al., Immune Stimulation by an Antisense Oligomer Complementary to the rev gene of HIV-1. <i>Biochemical Pharmacology</i> , Vol. 45, 10:2037-2043, 1993.							
*		Briskin M et al., Lipopolysaccharide-unresponsive mutant pre-B-cell lines blocked in NF-kappa B activation. <i>Mol Cell Biol</i> 10(1):422-5, Jan 1990.							
*		Chace, J. et al., Regulation of Differentiation in CD5+ and Conventional B Cells, <i>Clinical Immunology and Immunopathology</i> , (1993), 68:3:327-332.							

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		APPLICANT Krieg	
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*	Chang YN et al., The palindromic series I repeats in the simian cytomegalovirus major immediate-early promoter behave as both strong basal enhancers and cyclic AMP response elements. <i>J Virol</i> 64(1):264-77, Jan 1990.		
*	Chu RS et al., CpG oligodeoxynucleotides act as adjuvants that switch on T helper 1 (Th1) immunity... <i>J Exp Med</i> 186(10):1623-31, 17 Nov 1997.		
*	Cowdery JS et al., Bacterial DNA induces NK cells to produce IFN-gamma in vivo and increases the toxicity of lipopolysaccharides. <i>J Immunol</i> 156(12):4570-5, 15 Jun 1996.		
*	Crosby et al., The Early Responses Gene FGFI-C Encodes a Zinc Finger Transcriptional Activator and is a Member of the GCGGGGGCG (GSG) Element-Binding Protein Family. <i>Mol. Cell. Biol.</i> , 2:3835-3841, 1991.		
*	Crystal, Transfer of Genes to Humans: Early Lessons and Obstacles to Success. <i>Science</i> , Vol. 270, pp. 404-410, 1995.		
*	D'Andrea A et al., Interleukin 10 (IL-10) inhibits human lymphocyte interferon gamma-production by suppressing natural killer cell stimulatory factor/IL-12 synthesis in accessory cells. <i>J Exp Med</i> 178(3):1041-8, 1993.		
*	Englisch et al., Chemically Modified Oligonucleotides as Probes and Inhibitors, <i>Angew. Chem. Int. Ed. Engl.</i> , 30:613-629, 1991.		
*	Erb KJ et al., Infection of mice with Mycobacterium bovis-Bacillus Calmette-Guerin (BCG) suppresses allergen-induced airway eosinophilia. <i>J Exp Med</i> 187(4):561-9, 16 Feb 1998.		
*	Etlinger, Carrier sequence selection - one key to successful vaccines, <i>Immunology Today</i> , Vol. 13, 2:52-55, 1992.		
*	Fox RI, Mechanism of action of hydroxychloroquine as an antirheumatic drug. <i>Chemical Abstracts</i> , 120:15, Abstract No. 182630 (April 29, 1994).		
*	Froehler, B.C. et al., Synthesis of DNA via deoxynucleotide H-phosphonate intermediates, <i>Nucleic Acid Research</i> , 14(13):5399, 1986.		
*	Gura, T., Antisense Has Growing Pains. <i>Science</i> (1995), 270:575-576.		
*	Hadden J et al., Immunostimulants. <i>TIPS</i> , (1993), 141:169-174.		
*	Hadden J et al., Immunopharmacology, <i>JAMA</i> , (1992) 268:20:2964-2969.		
*	Halpern MD et al., Bacterial DNA induces murine interferon-gamma production by stimulation of interleukin-12 and tumor necrosis factor-alpha. <i>Cell Immunol</i> 167(1):72-8, 1996.		
*	Hatzfeld J., Release of Early Human Hematopoietic Progenitors from Quiescence by Antisense Transforming Growth Factor $\beta$ 1 or Rb Oligonucleotides, <i>J. Exp. Med.</i> , (1991) 174:925-929.		
*	Highfield PE, Sepsis: the More, the Murkier. <i>Biotechnology</i> , 12:828, August 12, 1994.		
*	Hoeffler JP et al., Identification of multiple nuclear factors that interact with cyclic adenosine 3',5'-monophosphate response element-binding protein and activating transcription factor-2 by protein-protein interactions. <i>Mol Endocrinol</i> 5(2):256-66, Feb 1991.		
*	Iguchi-Arigo SM and Shaffner W, CpG methylation of the cAMP-responsive enhancer/promoter sequence TGACGTCA abolishes specific factor binding as well as transcriptional activation. <i>Genes Dev</i> 3(5):612-9, May 1989.		
*	Iverson, P., et al., "Pharmacokinetics of an Antisense Phosphorothioate Oligodeoxynucleotide against rev from Human Immunodeficiency Virus Type 1 in the Adult male Rhesus Following Single Injections and Continuous Infusion", <i>Antisense Research and Development</i> , (1994), 4:43-52		
*	Ishikawa R et al., IFN induction and associated changes in splenic leukocyte distribution. <i>J Immunol</i> 150(9):3713-27, 1 May 1993		

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*		Jakway JP et al., Growth regulation of the B lymphoma cell line WEHI-231 by anti-immunoglobulin, lipopolysaccharide, and other bacterial products. <i>J Immunol</i> 137(7):2225-31, 1 Oct 1986.	
*		Jaroszewski JW and Cohen JS, Cellular uptake of antisense oligonucleotides. <i>Adv Drug Delivery Rev</i> 6(3):235-50, 1991.	
*		Kataoka, T. et al., Antitumor Activity of Synthetic Oligonucleotides with Sequences from cDNA Encoding Proteins of Mycobacterium bovis BCG, <i>Jpn. J. Cancer Res.</i> , 83:244, 1992.	
*		Kimura Y et al., Binding of Oligoguanylate to Scavenger Receptors Is Required for Oligonucleotides to Augment NK Cell Activity and Induce IFN, <i>J. Biochem.</i> , Vol. 116, 5:991-994, 1994.	
*		Kline JN et al., CpG motif oligonucleotides are effective in prevention of eosinophilic inflammation in a murine model of asthma. <i>J Invest Med</i> 44(7):380A, 1996.	
*		Kline JN et al., Immune redirection by CpG oligonucleotides. Conversion of a Th2 response to a Th1 response in a murine model of asthma. <i>J Invest Med</i> 45(3):282A, 1997.	
*		Kline JN et al., CpG oligonucleotides can reverse as well as prevent Th2-mediated inflammation in a murine model of asthma. <i>J Invest Med</i> 45(7):298A, 1997.	
*		Klinman DM et al., CpG motifs present in bacteria DNA rapidly induce lymphocytes to secrete interleukin 6, interleukin 12, and interferon gamma. <i>Proc Natl Acad Sci USA</i> 93(7):2879-83, 1996.	
*		Krajewski, W., et al., "A Monomeric Derivative of the Cellular Transcription Factor CREB Functions as a Constitutive Activator", <i>Molecular and Cellular Biology</i> , 14:11:7204-7210, (1994)	
*		Krieg AM, An innate immune defense mechanism based on the recognition of CpG motifs in microbial DNA. <i>J Lab Clin Med</i> 128(2):128-33, 1996.	
*		Krieg AM et al., Uptake of oligodeoxynucleotides by lymphoid cells is heterogeneous and inducible. <i>Antisense Res Dev</i> 1(2):161-71, Summer 1991.	
*		Krieg AM et al., Oligodeoxynucleotide modifications determine the magnitude of B cell stimulation by CpG motifs. <i>Antisense Nucleic Acid Drug Dev</i> 6(2):133-9, Summer 1996.	
*		Krieg AM et al., "Modification of antisense phosphodiester oligodeoxynucleotides by a 5' cholesteryl moiety increases cellular association and improves efficacy", <i>Proc. Natl. Acad. Sci.</i> , (1993), 90:1048-1052	
*		Krieg AM et al., "CpG DNA: A Pathogenic Factor in Systemic Lupus Erythematosus?", <i>Journal of Clinical Immunology</i> , (1995) 15:6:284-292.	
*		Krieg AM et al., "Phosphorothioate Oligodeoxynucleotides: Antisense or Anti-Protein?", <i>Antisense Research and Development</i> , (1995), 5:241	
*		Krieg AM et al., "Leukocyte Stimulation by Oligodeoxynucleotides", <i>Applied Antisense Oligonucleotide Technology</i> , (1998), 431-448	
*		Krieg AM et al., CpG motifs in bacterial DNA trigger direct B-cell activation. <i>Nature</i> 374:546-9, 1995.	
*		Krieg AM et al., "The role of CpG dinucleotides in DNA vaccines", <i>Trends in Microbiology</i> , Vol. 6, pp. 23-27, Jan 1998.	
*		Krieg AM et al., "A Role for Endogenous Retroviral Sequences in the Regulation of Lymphocyte Activation, the <i>Journal of Immunology</i> , Vol. 143, 2448-2451,	
*		Kuramoto et al., Oligonucleotide Sequences Required for Natural Killer Cell Activation, <i>Jpn. J. Cancer Res.</i> , 83:1128-1131, November 1992.	
*		Kwok, R., et al., "Nuclear protein CBP is a coactivator for the transcription factor CREB", <i>Nature</i> , 370:223-226, (1994)	
*		Lacour, J., Clinical Trials Using Polyadenylic-Polyuridylic Acid as an Adjuvant to Surgery in Treating Different Human Tumors, <i>J. Biological Response Modifiers</i> , 4(5):538, 1985.	



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		FILING DATE July 14, 2003	GROUP Not Yet Assigned
*	Lee, K., et al., "Transcriptional regulation by CREB and its relatives", <i>Biochemica et Biophysica Acta</i> , 1174:221-233, (1993)		
*	Leonard et al., Conformation of Guanine 8-Oxoadenine Base Pairs in the Crystal Structure of d(CGCGAATT(08A)GCG). <i>Biochemistry</i> , 31(36):8415-8420, 1992.		
*	Macfarlane DE and Manzel L, Antagonism of immunostimulatory CpG-oligodeoxynucleotides by quinacrine, chloroquine, and structurally related compounds. <i>J Immunol</i> 160(3):1122-31, Feb 1 1998.		
*	Mastrangelo et al. <i>Seminars in Oncology</i> . Vol. 23, 1:4-21, 1996.		
*	Matson S and Krieg AM, Nonspecific suppression of [3H]thymidine incorporation by "control" oligonucleotides. <i>Antisense Res Dev</i> 2(4):325-30, Winter 1992.		
*	McIntyre KW et al., A sense phosphorothioate oligonucleotide directed to the initiation codon of transcription factor NF-kappa B p65 causes sequence-specific immune stimulation. <i>Antisense Res Dev</i> 3(4):309-22, Winter 1993.		
*	Messina et al., The Influence of DNA Structure on the <i>in vitro</i> Stimulation of Murine Lymphocytes by Natural and Synthetic Polynucleotide Antigens. <i>Cellular Immunology</i> , 147:148-157, 1993.		
*	Messina et al., Stimulation of <i>in vitro</i> Murine Lymphocyte Proliferation by Bacterial DNA. <i>J. Immunol.</i> , Vol. 147, 6:1759-1764, September 15, 1991.		
*	Mojcik, C., et al., "Administration of a Phosphorothioate Oligonucleotide Antisense Murine Endogenous Retroviral MCF env Causes Immune Effect in vivo in a Sequence-Specific Manner", <i>Clinical Immunology and Immunopathology</i> , (1993), 67:2:130-136		
*	Mottram et al., A novel CDC2-related protein kinase from leishmania mexicana LmmCRK1 is post-translationally regulated during the life cycle. <i>J. Biol. Chem.</i> 268:28, 21044-21052 (October 1993).		
*	<i>New England BIOLABS 1988-1989 Catalog</i>		
*	Nyce JW and Metzger WJ, DNA antisense therapy for asthma in an animal model. <i>Nature</i> 385:721-725, 20 Feb 1997.		
*	Paca-Uccaralertkun, S., et al., "In Vitro Selection of DNA Elements Highly Responsive to the Human T-Cell Lymphotropic Virus Type I Transcriptional Activator, Tax, <i>Molecular and Cellular Biology</i> , 14:1:456-462, (1994)		
*	Pisetsky, D., "Stimulation of in vitro proliferation of murine lymphocytes by synthetic oligodeoxynucleotides", <i>Molecular Biology Reports</i> , (1993) 18:217-221		
*	Pisetsky et al., Stimulation of Murine Lymphocyte Proliferation by a Phosphorothioate Oligonucleotide with Antisense Activity for Herpes Simplex Virus. <i>Life Science</i> , Vol. 54, pp. 101-107 (1994).		
*	Pisetsky, The Immunological Properties of DNA, <i>The Journal of Immunology</i> , pp. 421-423 (1996).		
*	Pisetsky, Immunological Consequences of Nucleic Acid Therapy, <i>Antisense Research and Development</i> , 5:219-225 (1995).		
*	Raz E et al., Preferential induction of a Th1 immune response and inhibition of specific IgE antibody formation by plasmid DNA immunization. <i>Proc Natl Acad Sci USA</i> 93(10):5141-5, 14 May 1996.		
*	Roman M et al., Immunostimulatory DNA sequences function as T helper-1-promoting adjuvants. <i>Nat Med</i> 3(8):849-54, Aug 1997.		
*	Sarmiento, U., et al., "In Vivo Toxicological Effects of rel A Antisense Phosphorothioates in CD-1 Mice", <i>Antisense Research and Development</i> , 4:99-107, (1994)		
*	Sato et al., Immunostimulatory DNA Sequences Necessary for Effective Intradermal Gene Immunization, <i>Science</i> , Vol. 273, pp. 352-354, 1996.		

FORM PTO-1449 (Modified)		ATTY. DOCKET NO.	SERIAL NO
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT		C01039.70077.US	Not Yet Assigned
		APPLICANT Krieg	
		FILING DATE July 14, 2003	GROUP Not Yet Assigned
*	Schnell et al., Identification and characterization of a <i>Saccharomyces cerevisiae</i> gene (PAR1) conferring resistance to iron chelators. <i>Eur. J. Biochem.</i> , 200:487-493.		
*	Schwartz DA et al., Endotoxin responsiveness and grain dust-induced inflammation in the lower respiratory tract. <i>Am J Physiol</i> 267(5 Pt 1):L609-17, 1994.		
*	Schwartz DA et al., The role of endotoxin in grain dust-induced lung disease. <i>Am J Respir Crit Care Med</i> 152(2):603-8, 1995.		
*	Schwartz DA et al., CpG motifs in bacterial DNA cause inflammation in the lower respiratory tract. <i>J Clin Invest</i> 100(1):68-73, 1 Jul 1997.		
*	Shirakawa T et al., The inverse association between tuberculin responses and atopic disorder. <i>Science</i> 275(5296):77-9, 3 Jan 1997.		
*	Sparwasser T et al., Macrophages sense pathogens via DNA motifs: induction of tumor necrosis factor-alpha-mediated shock. <i>Eur J Immunol</i> 27(7):1671-9, Jul 1997.		
*	Stein CA et al., Oligonucleotides as inhibitors of gene expression: a review. <i>Cancer Research</i> , 48:2659-2668, 1988.		
*	Stull et al., Antigene, Ribozyme, and Aptamer Nucleic Acid Drugs: Progress and Prospects, <i>Pharmaceutical Res.</i> , Vol. 12, 4:465-483, 1995.		
*	Subramanian et al., Theoretical Considerations on the "Spine of Hydration" in the Minor Groove of d(CGCGAATTCGCG) d(GCGCTTAAGCGC): Monte Carlo Computer Simulation. <i>Proc. Nat'l. Acad. Sci. USA</i> , 85:1836-1840, 1988.		
*	Tanaka T et al., An antisense Oligonucleotide complementary to a sequence in IG2b increases G2b germline transcripts stimulates B cell DNA synthesis and inhibits immunoglobulin secretion. <i>J. Exp. Med.</i> , 175:597-607, 1992.		
*	Thorne PS., Experimental grain dust atmospheres generated by wet and dry aerosolization techniques. <i>Am J Ind Med</i> 25(1):109-12, 1994.		
*	Tokunaga T et al., Synthetic Oligonucleotides with Particular Base Sequences form the cDNA Encoding Proteins of <i>Mycobacterium bovis</i> BCG Induce Interferons and Activate Natural Killer Cells, <i>Microbiol. Immunol.</i> , Vol. 36, 1:55-66, 1992.		
*	Tokunaga et al., A Synthetic Single-Stranded DNA, Poly (dG, dC), Induces Interferon $\alpha/\beta$ and $\gamma$ , Augments Natural Killer Activity and Suppresses Tumor Growth. <i>Jpn. J. Cancer Res.</i> , 79:682-686, June 1988.		
*	Tsukada, J., et al., "Transcriptional Factors NF-IL6 and CREB Recognize a Common Essential Site in the Human prointerleukin 1 $\beta$ Gene", <i>Molecular and Cellular Biology</i> , 14:11:7285-7297, (1994)		
*	Uhlmann et al., Antisense Oligonucleotides: A New Therapeutic Principle. <i>Chemical Reviews</i> , 90:543-584, 1990.		
*	Wagner RW, Gene inhibition using antisense oligodeoxynucleotides. <i>Nature</i> , 372:L333-335, 1994.		
*	Wallace et al., Oligonucleotide probes for the screening of recombinant DNA libraries. <i>Methods in Enzymology</i> , 152:432-442 (1987).		
*	Weiss R., Upping the Antisense Ante: Scientists bet on profits from reverse genetics. <i>Science</i> , 139:108-109, 1991.		
*	Whalen R, DNA Vaccines for Emerging Infection Diseases: What If?, <i>Emerging Infectious Disease</i> , Vol. 2, 3:168-175, 1996.		
*	Wu GY et al., Receptor-mediated gene delivery and expression in vivo. <i>J. Biol. Chem.</i> , 263:14621-14624, 1988.		
*	Wu-Pong S., Oligonucleotides: Opportunities for Drug Therapy and Research. <i>Pharmaceutical Technology</i> , 18:102-114, 1994.		

FORM PTO-1449 (Modified)		ATTY. DOCKET NO.	SERIAL NO
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT		C01039.70077.US	Not Yet Assigned
APPLICANT Krieg			
		FILING DATE July 14, 2003	GROUP Not Yet Assigned
*		Yamamoto S et al., DNA from bacteria, but not from vertebrates, induces interferons, activates natural killer cells and inhibits tumor growth. <i>Microbiol Immunol</i> 36(9):983-97, 1992.	
*		Yamamoto S et al., <i>In vitro</i> augmentation of natural killer cell activity and production of interferon-alpha/beta and -gamma with deoxyribonucleic acid fraction from <i>Mycobacterium bovis</i> BCG. <i>Jpn J Cancer Res</i> 79:866-73, Jul 1988.	
*		Yamamoto S., Mode of Action of Oligonucleotide Fraction Extracted from <i>Mycobacterium bovis</i> BCG, <i>Kekkaku</i> , Vol. 69, 9:29-32, 1994.	
*		Yamamoto S et al., Unique Palindromic Sequences in Synthetic Oligonucleotides are Required to Induce INF and Augment INF-Mediated Natural Killer Activity. <i>J. Immunol.</i> , Vol. 148, 12:4072-4076, June 15, 1992.	
*		Yamamoto T et al., Ability of Oligonucleotides with Certain Palindromes to Induce Interferon Production and Augment Natural Killer Cell Activity is Associated with Their Base Length. <i>Antisense Res. and Devel.</i> , 4:119-123, 1994.	
*		Yamamoto et al., Lipofection of Synthetic Oligodeoxyribonucleotide Having a Palindromic Sequence AACGTT to Murine Splenocytes Enhances Interferon Production and Natural Killer Activity. <i>Microbiol. Immunol.</i> , Vol. 38, 10:831-836, 1994.	
*		Yamamoto T et al., Synthetic Oligonucleotides with Certain Palindromes Stimulate Interferon Production of Human Peripheral Blood Lymphocytes <i>in vitro</i> . <i>Jpn. J. Cancer Res.</i> , 85:775-779, 1994.	
*		Yi, Ae-Kyung et al., IFN- $\gamma$ Promotes IL-6 and IgM Secretion in Response to CpG Motifs in Bacterial DNA and Oligonucleotides, <i>The Journal of Immunology</i> , pp. 558-564 (1996).	
*		Yi, Ae-Kyung et al., Rapid Immune Activation by CpG Motifs in Bacterial DNA, <i>The Journal of Immunology</i> , pp. 5394-5402 (1996).	
*		Zelphati, O. et al., Inhibition of HIV-1 Replication in Cultured Cells with Antisense Oligonucleotides Encapsulated in Immunoliposomes, <i>Antisense Res. and Devel.</i> , 3:323, 1993.	
*		Zhao Q et al., Stage-specific oligonucleotide uptake in murine bone marrow B-cell precursors. <i>Blood</i> 84(11):3660-6, 1 Dec 1994.	
*		Zhao Q et al., Comparison of cellular binding and uptake of antisense phosphodiester, phosphorothioate, and mixed phosphorothioate and methylphosphonate oligonucleotides. <i>Antisense Res Dev</i> 3(1):53-66, Spring 1993.	

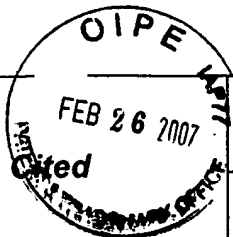
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EXAMINER <i>Smith, E. J.</i>	DATE CONSIDERED 9-18-06
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# **Notice of References Cited**



Application/Control No.

10/619,279

Applicant(s)/Patent Under  
Reexamination  
KRIEG, ARTHUR M.

Examiner

Janet L. Epps-Ford

Art Unit

1633

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## **U.S. PATENT DOCUMENTS**

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-6,239,116	05-2001	Krieg et al.	514/44
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
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	L	US-			
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## **FOREIGN PATENT DOCUMENTS**

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

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